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Odorant Similarity in the Mouse Olfactory Bulb

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It is widely held that odorant chemical features are mapped onto the olfactory epithelium (1, 2) and bulb (3), such that similar odorants activate common receptors and glomeruli. After applying ultra-high-resolution G-CaMP2 imaging to the olfactory bulb, Ma et al (4) failed to identify a correlation between odorant pairwise structural differences and pairwise neuronal response differences (Fig. 4E in Ma et al). They concluded that: "response similarity was not dictated by structural similarity of the odors, and vice versa".

Ma et al made their raw data available for download, allowing us to identify several analysis decisions that may underlie their null result. First, Ma et al did not normalize the values of the various physicochemical descriptors. These measurements use vastly different scales, and their normalization is paramount for meaningful analysis. Second, Ma et al estimated pairwise structural similarity using Pearson correlations, rather than the previously used Euclidian distance (5). To estimate whether these decisions contributed to the lack of correlation reported by Ma et al, we repeated the full analysis. We measured odorant structural pairwise distances using Euclidian distance (supplementary data contains all the normalized physicochemical variables for all the Ma et al odors, as well as 1307 odors to form a space for representation), and odorant neural pairwise distance using the Pearson correlation. To allow correlational analysis, we ignored experiments with less than 10 activating odorants (19 of 75 experiments) (5). In contrast to the null correlation reported by Ma et al, we observed significant correlations in 11 of 12 mice (binomial, $p < 0.003$), as well as in 40 of 56 experiments (binomial, $p < 0.0006$), ranging from $r = 0.65$, $p < 10^{-11}$, to $r = 0.01$, $p = \text{ns}$ (Fig. 1a).

Some of the experiments conducted by Ma et al provided more information than others. Particularly, the first three mice had complete datasets containing many more glomeruli (59, 44 and 61, compared to 17.4 ± 2 in the rest), and odors (94, 68 and 97, compared to 64 ± 24 in the rest). We therefore used these animals for continued in-depth analysis. We hypothesized that including odorants which failed to activate any of the recorded glomeruli may have skewed the results reported by Ma et al. To test this, we plotted the correlation between odorant structure and neural activity as a function of a threshold applied to the neuronal response. In other words, we removed successively larger numbers of odors that had only sporadic responding glomeruli. We observed that in all three animals, once this threshold assured that $\sim 10\%$ or more of the glomeruli were involved in each response (removal of 51, 43 and 43 odors respectively), the correlation between odorant structure and neural activity increased, particularly in the low concentration experiments (from $r = 0.12$; 0.28 ; and 0.07 to $r = 0.54$; 0.79 ; and 0.18 respectively, all $p < 0.0001$) (Fig. 1b). In other words, once we omitted odors with minimal overall response, an overwhelming correlation emerged (Fig. 1c). We conclude, in contrast to Ma et al, that structurally similar odors activate common sets of glomeruli.

Figure 1: Odorant Similarity in the Mouse Olfactory Bulb

A. Correlation between odorant pairwise structural similarity (Euclidian distance) and neural response similarity (Pearson correlation) in all experiments/concentrations reported by Ma et al. * < 0.05 ; ** < 0.005 ; *** < 0.0005 . B. Deleting odors with no responding glomeruli reveals strong correlations at low concentrations. C. Correlation between neural response distance and structural distance in the low concentration experiments (60 odors) in the three complete dataset mice.

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Figure 1

